

AMENDMENTS TO THE CLAIMS:

Please substitute currently amended claim numbers 1 and 17 for the original claims having the same claim numbers.

Please add for consideration new claim numbers 54- 59.

1. (currently amended) A genetically-modified non-human mammal containing a genetic construct comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, ~~polynucleotide sequence encoding an immunoglobulin~~ and at least one detectable protein, ~~wherein said construct comprises the CH1, CH2 and G1 exons spliced together to make the constant region of the secreted form of the immunoglobulin molecule,~~ wherein said non-human mammal is capable of expressing at least one chimeric immunoglobulin gene comprising a polynucleotide sequence encoding at least one detectable protein or peptide fused with a gene expressing an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, wherein antibodies secreted by immune cells of said genetically-modified mammal comprise said at least one detectable protein or peptide.

2. (previously presented) The genetically-modified non-human mammal of claim 1 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide.

3. (previously presented) The genetically-modified non-human mammal of claim 2 wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide is located in exon G1.

4. (previously presented) The genetically-modified non-human mammal of claim 1 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween.
5. (previously presented) The genetically-modified non-human mammal of claim 4 wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker therebetween is located in exon G1.
6. (previously presented) The genetically-modified non-human mammal of claim 1 wherein said immunoglobulin heavy chain gene is selected from the group consisting of IgG, IgM, IgD and IgA.
7. (previously presented) The genetically-modified non-human mammal of claim 1 wherein an immunoglobulin molecule secreted by immune cells of said genetically-modified mammal comprises at least one detectable protein or peptide in the heavy chain of said immunoglobulin molecule.
8. (previously presented) The genetically-modified non-human mammal of claim 1 wherein an immunoglobulin molecule secreted by immune cells of said genetically-modified mammal comprises at least one detectable protein or peptide in the light chain of said immunoglobulin molecule.
9. (previously presented) The genetically-modified non-human mammal of claim 1 wherein an immunoglobulin molecule secreted by immune cells of said genetically-modified mammal comprises at least one detectable protein or peptide in the heavy chain and at least one detectable protein or peptide in the light chain of said immunoglobulin molecule.

10. (previously presented) The genetically-modified non-human mammal of claim 1 wherein at least one said detectable protein or polypeptide is capable of quenching fluorescence.

11. (previously presented) The genetically-modified non-human mammal of claim 1 wherein said at least one detectable protein or peptide is an autofluorescent protein or peptide, a visibly-detectable protein or peptide, an enzymatically active protein or peptide, a protein or peptide capable of interacting with another molecule to produce a detectable product, wherein said protein or peptide capable of interacting with another molecule to produce a detectable product is selected from the group consisting of an intein, a biotin-binding subunit of streptavidin or avidin, a His tag, or a chitin-binding domain, or any combination thereof, and wherein said detectable protein may be a single detectable protein or a plurality of detectable proteins, in tandem or not in tandem, optionally separated from the immunoglobulin portion of the polypeptide by one or more linker sequences.

12. (previously presented) The genetically-modified non-human mammal of claim 11 wherein said at least one detectable protein is an autofluorescent protein or peptide.

13. (previously presented) The genetically-modified non-human mammal of claim 11 wherein said autofluorescent protein or peptide is selected from the group consisting of green fluorescent protein, cyan fluorescent protein, yellow fluorescent protein, red fluorescent protein, and a fluorescent analog or fragment of any of the foregoing.

14. (previously presented) The genetically-modified non-human mammal of claim 12 wherein said autofluorescent protein is green fluorescent protein.

15. (previously presented) The genetically-modified non-human mammal of claim 11 wherein said at least one detectable protein is a combination of an autofluorescent protein or peptide and an enzymatically-active protein or peptide.

16. (previously presented) The genetically-modified non-human mammal of claim 15 wherein said at least one detectable protein is a combination of green fluorescent protein and alkaline phosphatase.

17. (currently amended) A genetically-modified immune cell produced *in vivo* and isolated from the genetically modified non-human mammal of claim 1 comprising a fusion polynucleotide, said fusion polynucleotide comprising sequence encoding an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, and at least one detectable protein, wherein said at least one detectable protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween, and wherein said immune cell is capable of expressing at least one chimeric immunoglobulin gene comprising a polynucleotide sequence encoding at least one detectable protein or peptide fused with a gene expressing an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, wherein antibodies secreted by said genetically-modified immune cell comprise said at least one detectable protein or peptide.

18. (original) The genetically-modified immune cell of claim 17 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide.

19. (original) The genetically-modified immune cell of claim 18 wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide is located in exon G1.

20. (canceled)

21. (previously presented) The genetically-modified immune cell of claim 17, wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker therebetween is located in exon G1.

22. (original) The genetically-modified immune cell of claim 17 wherein said immunoglobulin heavy chain gene is selected from the group consisting of IgG, IgM, IgD and IgA.

23. (original) The genetically-modified immune cell of claim 17 wherein an immunoglobulin molecule secreted by said immune cell comprises at least one detectable protein or peptide in the heavy chain of said immunoglobulin molecule.

24. (original) The genetically-modified immune cell of claim 17 wherein an immunoglobulin molecule secreted by said genetically-modified immune cells comprises at least one detectable protein or peptide in the light chain of said immunoglobulin molecule.

25. (original) The genetically-modified immune cell of claim 17 wherein an immunoglobulin molecule secreted by said genetically-modified immune cells comprises at least one detectable protein or peptide in the heavy chain and at least one detectable protein or peptide in the light chain of said immunoglobulin molecule.

26. (original) The genetically-modified immune cell of claim 17 wherein at least one said detectable protein or polypeptide is capable of quenching fluorescence.

27. (previously presented) The genetically-modified immune cell of claim 17 wherein said at least one detectable protein or peptide is an autofluorescent protein or peptide, a visibly-detectable protein or peptide, an enzymatically active protein or peptide, a protein or peptide capable of interacting with another molecule to produce a detectable product, wherein said protein or peptide capable of interacting with another molecule to produce a detectable product is

selected from the group consisting of an intein, a biotin-binding subunit of streptavidin or avidin, a His tag, a chitin-binding domain, or any combination thereof.

28. (original) The genetically-modified immune cell of claim 27 wherein said at least one detectable protein is an autofluorescent protein or peptide.

29. (original) The genetically-modified immune cell of claim 28 wherein said autofluorescent protein or peptide is selected from the group consisting of green fluorescent protein, red fluorescent protein, and a fluorescent analog or fragment of any of the foregoing.

30. (original) The genetically-modified immune cell of claim 29 wherein said autofluorescent protein is green fluorescent protein.

31. (original) The genetically-modified immune cell of claim 27 wherein said at least one detectable protein is a combination of an autofluorescent protein or peptide and an enzymatically-active protein or peptide.

32. (original) The genetically-modified immune cell of claim 31 wherein said at least one detectable protein is a combination of green fluorescent protein and alkaline phosphatase.

33. (withdrawn) A hybridoma comprising the genetically-modified immune cell of claim 17.

34. (withdrawn) A chimeric, detectably-labeled immunoglobulin molecule comprising at least one detectable protein or peptide fused with the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, or any combination thereof.

35. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 34 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide.

36. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 35 wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide is located in exon G1.

37. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 35 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween.

38. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 37 wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker therebetween is located in exon G1.

39. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 34 wherein said immunoglobulin heavy chain gene is selected from the group consisting of IgG, IgM, IgD and IgA.

40. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 34 comprising at least one detectable protein or peptide in the heavy chain of said immunoglobulin molecule.

41. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 34 comprising at least one detectable protein or peptide in the light chain of said immunoglobulin molecule.

42. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 34 comprising at least one detectable protein or peptide in the heavy chain and at least one detectable protein or peptide in the light chain of said immunoglobulin molecule.

43. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 42 wherein at least one said detectable protein or polypeptide is capable of quenching fluorescence.

44. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 34 wherein said at least one detectable protein or peptide is an autofluorescent protein or peptide, a visibly-detectable protein or peptide, an enzymatically active protein or peptide, a protein or peptide capable of interacting with another molecule to produce a detectable product, or any combination thereof.

45. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 44 wherein said at least one detectable protein is an autofluorescent protein or peptide.

46. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 45 wherein said autofluorescent protein or peptide is selected from the group consisting of green fluorescent protein, red fluorescent protein, and a fluorescent analog or fragment of any of the foregoing.

47. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 46 wherein said autofluorescent protein is green fluorescent protein.

48. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 44 wherein said at least one detectable protein is a combination of an autofluorescent protein or peptide and an enzymatically-active protein or peptide.

49. (withdrawn) The chimeric, detectably-labeled immunoglobulin molecule of claim 48 wherein said at least one detectable protein is a combination of green fluorescent protein and alkaline phosphatase.

50. (withdrawn) A method for producing a quantity of detectably-labelled polyclonal antibodies comprising the steps of



- a) providing a genetically-modified mammal in accordance with claim 1;
- b) immunizing said genetically-modified mammal with a preselected immunogen, wherein said genetically-modified mammal generates antibodies to said immunogen, wherein antibodies secreted by immune cells of said genetically-modified mammal comprise said at least one detectable protein or peptide; and
- c) isolating said detectably-labelled antibodies from said genetically-modified mammal.

51. (withdrawn) A method for producing a quantity of detectably-labelled monoclonal antibodies comprising the steps of

- a) preparing a genetically-modified mammal in accordance with claim 1;
- b) immunizing said genetically-modified mammal with a preselected immunogen, wherein immune cells of said genetically-modified mammal generate antibodies to said immunogen, wherein antibodies secreted by said immune cells comprise said at least one detectable protein or peptide; and
- c) immortalizing antibody-producing immune cells isolated from said genetically-modified mammal;
- d) selecting immortalized immune cells isolated from said genetically-modified mammal that secrete antibodies specific to said immunogen; and
- e) preparing a quantity of detectably-labeled monoclonal antibodies from said selected immune cells.

52. (previously presented) A genetically-modified non-human mammal capable of producing a detectably-labeled immunoglobulin in response to immunization by an antigen, the genome of said non-human mammal comprising at least one fusion polynucleotide consisting of a polynucleotide sequence encoding at least one detectable protein or peptide fused with a gene selected from the group consisting of the kappa immunoglobulin light chain gene, the lambda immunoglobulin light chain gene, an

immunoglobulin heavy chain gene, and any combination thereof, wherein antibodies secreted by immune cells of said genetically-modified non-human mammal comprise said at least one detectable protein or peptide.

53. (withdrawn) A chimeric, detectably-labeled immunoglobulin molecule comprising at least one fluorescent protein or peptide and at least one fluorescence-quenching protein or peptide fused with a component of said immunoglobulin molecule independently selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof.

54. (new) A genetically-modified non-human mammal containing a genetic construct comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, and at least one detectable protein, wherein said non-human mammal is capable of expressing said fusion polynucleotide, and wherein antibodies secreted by immune cells of said genetically-modified mammal comprise said at least one detectable protein or peptide, wherein said at least one said detectable protein or peptide is capable of quenching fluorescence.

55. (new) A genetically-modified non-human mammal containing a genetic construct comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, and at least one detectable protein, wherein said non-human mammal is capable of expressing said fusion polynucleotide, and wherein antibodies secreted by immune cells of said genetically-modified mammal comprise said at least one detectable protein or peptide, wherein said at least one said detectable protein or peptide is a combination of an autofluorescent protein or peptide

and an enzymatically-active protein or peptide.

56. (new) A genetically-modified non-human mammal containing a genetic construct comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, and at least one detectable protein, wherein said non-human mammal is capable of expressing said fusion polynucleotide, and wherein antibodies secreted by immune cells of said genetically-modified mammal comprise said at least one detectable protein or peptide, wherein said at least one said detectable protein or peptide is a combination of green fluorescent protein and alkaline phosphatase.

57. (new) A genetically-modified immune cell produced *in vivo* and isolated from the genetically modified non-human mammal of claim 54, comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, and at least one detectable protein, wherein said at least one detectable protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween, and wherein said immune cell is capable of expressing said fusion polynucleotide, and wherein antibodies secreted by said genetically-modified immune cell comprise said at least one detectable protein or peptide, wherein said at least one detectable protein or peptide is capable of quenching fluorescence.

58. (new) A genetically-modified immune cell produced *in vivo* and isolated from the genetically modified non-human mammal of claim 55, comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination

thereof, and at least one detectable protein, wherein said at least one detectable protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween, wherein said immune cell is capable of expressing said fusion polynucleotide, and wherein antibodies secreted by said genetically-modified immune cell comprise said at least one detectable protein or peptide, wherein said at least one detectable protein or peptide is a combination of an autofluorescent protein or peptide and an enzymatically-active protein or peptide.

59. (new) A genetically-modified immune cell produced *in vivo* and isolated from the genetically modified non-human mammal of claim 56, comprising a fusion polynucleotide, said fusion polynucleotide comprising an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, and at least one detectable protein, wherein said at least one detectable protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween, wherein said immune cell is capable of expressing said fusion polynucleotide, and wherein antibodies secreted by said genetically-modified immune cell comprise said at least one detectable protein or peptide, wherein said at least one detectable protein or peptide is a combination of green fluorescent protein and alkaline phosphatase.